live-stock may in the future assume if it is now neglected and allowed to gain a permanent place on this Continent. In view of our past experiences in the matter of international commercial jealousies and reprisals against American cattle by certain European nations, under the pretense of sanitary safeguards, the United States Government may well give serious heed to the possibility of furnishing to countries commercially hostile to us a plausible pretext for the exclusion of American animals, if by its present negligence it allows hydatid disease to become endemic and widespread in this country, as it is in Germany, Australia, the Argentine Republic, and many other parts of the civilized world.

In conclusion, we wish to acknowledge our indebtedness for notes of unpublished cases to various gentlemen mentioned in the summary of cases, and, in particular, to Dr. H. H. Chown, of Winnipeg, for his private notes of a large number of cases in Icelanders, and to Dr. Frederick A. Packard, of Philadelphia, for his generosity in placing at our disposal his references to cases which he had been systematically collecting from the literature with a view to ultimate publication.

RECENT VIEWS OF THE ORIGIN AND NATURE OF HERPES ZOSTER.

By Arthur Van Harlingen, M.D.,
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Some years ago my friend Dr. Curtin called my attention to some cases observed by him, which seemed to point to the occurrence of herpes zoster on the pleura, the peritoneum, and in the articulations. He asked me whether I knew of any similar cases. I had not had any personal experience, but determined to examine the literature of herpes zoster with this point in view. It is only recently that I have had the opportunity of doing this, but, although references to the subject are scanty, quite a number of cases have been published which go to confirm Dr. Curtin's observations.

At the same time I have found so much of interest in scattered monographs of recent date that I have thought well to give some account of the views generally prevalent among dermatologists and neurologists regarding the nature of herpes zoster.[1] In order to do this satisfactorily, it seems desirable to give a hasty sketch of what is known regarding the pathology of the disease and of the various theories as to its origin.

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[1] Dr. Curtin's views are stated in several monographs. "Is Herpes Zoster a Cause of Pleurisy and Peritonitis?" Sanitarian, December, 1890, and in other publications. Some valuable observations will be found in his latest contribution to the subject, to appear in the next number of the Journal.

Barth, in an account of herpes zoster, or, as I shall call it for convenience, zoster, says that Parrot, in 1857, advanced the theory of zoster as a secondary disease, subordinate to a neuralgia, and Charcot, in 1859, called attention to a case, the first recorded, where zoster followed an injury. In 1861 Bärensprung, in his classical paper, developed the idea of the nervous origin of zoster, and attributed it to a disease of the ganglionic system, an irritation of the spinal ganglia, or of the Gasserian ganglia, while admitting that peripheral irritation of a nerve might result in a limited outbreak of the eruption.

In 1864 Mitchell, Morehouse, and Keen showed that irritation and not section of a nerve was the cause of zoster and similar eruptions. Later it was shown that compression by tumors, etc., might result in zoster on the distribution of the implicated nerve.

In 1872 Charcot reported a case of double zoster of the trunk following acute myelitis of the anterior cornua, and later reported cases of zoster occurring in connection with locomotor ataxia.

The mode of action of the morbid influence through the nerve on the skin was early made the subject of speculation, and several theories have been brought forward. What was known as the *vasomotor theory* assumed that the contraction, expansion, or paralysis of bloodvessels, and the consequent increase or decrease in the amount of nourishment brought to the cells, might lead to nutritive changes. This failed of experimental proof.

Samuel suggested a theory of *trophic nerve fibres* which was ingenious, but the existence of such fibres never having been proved, the theory fell to the ground.

The theory of the *trophic action of sensory nerves* attributes to the ordinary sensory and motor nerve fibres those functions for which Samuel had provided a special group of nerves. The nervous system acts on the nutrition of the anatomical elements by maintaining their functional activity. Trophic influence is thus transmitted to the skin and mucous membranes by the sensory nerves. Any alteration in the sensory fibres would result in the enfeeblement of the trophic influence of spinal and Gasserian ganglia upon these fibres and probably through their mediation on certain elements of the skin itself.

If this is the case we must admit that the weakening of this trophic influence would create a state of least resistance, or of greater vulnerability in those parts of the skin connected with the peripheral extremities of the affected sensory nerves.

Under these conditions, an irritant local cause, such as pressure, rubbing of the skin by clothing, or even contact of the air, might determine the appearance of the herpetic eruption, and, as would appear from recent observations, a microbic invasion could also occur.

Although this theory is attractive, and, if well founded, would explain the pathology of zoster better than any yet brought forward, it has not as yet been proved, and remains a theory like the others.

The simplest and most plausible theory of the production of zoster, and one, indeed, which must account for a certain number of cases, is that of *propagated neuritis*. This supposes that zoster is simply the result of an inflammatory irritation transmitted by continuity of tissue from a nerve twig, or branch, to the cutaneous elements among which it is distributed.

I may say here in passing, that these theories take for granted that all zosteriform eruptions are of the same nature, and that each belongs to a specific affection: herpes zoster. In the present state of our knowledge, however, this is by no means universally admitted. We may have a specific herpes zoster, as we believe there is a specific pemphigus, while at the same time we may have various zosteroid eruptions, as we have various bullar or pemphigoid eruptions, which may arise from various causes.

Such, at least, is the generally prevalent belief among the dermatologists of to-day.

At the time Barth wrote, discussions upon the etiology and pathology of zoster seemed premature. Zoster was to be recognized as the cutaneous expression of a nervous disturbance, irritative in character, affecting, sometimes the peripheral sensory nerves, and sometimes the spinal and cranial ganglia. Sometimes resulting from an injury, as contusion or compression of a nerve, sometimes as the result of cold, or under the influence of a general perturbation of the system.

The nerve disturbance might at times be so slight as not to affect perceptibly the anatomical integrity or the functions of the nerve fibres, and might show itself only by the cutaneous eruption.

At other times, however, and especially in the old, this slight initial disturbance might prelude a destructive neuritis, which might give rise to anæsthesia, rebellious neuralgias, and various other disorders of sensation so common as the result of severe zoster.

Although, most commonly, the morbid process produces only slight skin lesions, the irritation might extend to other organs innervated by the same nerves, and might determine grave and irreparable disorders. Ulceration of the cornea, as observed by Hutchinson and Hybord many years ago, and which is an occasional accompaniment of ophthalmic zoster, was one of the first of these complications to attract attention. Jouffroy pointed out that the neuritis of zoster may be propagated to neighboring nerves, and might cause atrophy of certain muscles. Such was the position of the zoster question as stated by Barth in his article, to which reference has been made. He hazarded, however, the suggestion that visceral organs might be attacked under the influence of the same cause as that producing the zoster in a given case, and referred to the opinion of Fernet, that certain pneumonias may be the expression of a sort of zoster of the pneumogastric nerve.

This prophecy, put forth by Barth twenty years ago, has been verified by subsequent clinical observations. A large number of cases of visceral disorders of various kinds in connection with zoster have been reported of late years. Pitres and Vaillard, Leroux, Potain, Huchard, Chandeleux, Mongour and Michel, Cantrell, Curtin, and others have shown the concurrence of zoster with tuberculosis, pleurisy, peritonitis, etc. Palm reported the case of an infant with bilateral zoster of the third branch of the trigeminal, which developed on the third day of a follicular angina. Hervonet reported a case of cervicobrachial zoster, accompanied by paresis of the arm, and, in addition, incomplete facial paralysis and ptosis. The various symptoms occurred simultaneously and, as will be observed, in different nerve tracts.

While these and similar cases continued to appear, other observations were published, going to show a close connection between zoster and various infective diseases. Gaucher and Barbe wrote on zoniform syphilides, Julien on zona and syphilis, and Spillman and Etienne published observations of a similar character. In the cases reported by the first of these writers, the distribution, as I understand, rather than the character of the lesions, lead to its denomination of zoniform, but the point of interest lies in the suggestion of the authors that the lesions had been produced, in all probability, under the influence of the pathogenic agent of syphilis or of its toxin upon the spinal axis.

Cancer, otherwise than through the direct influence of pressure from the new growth, has been suggested as a cause of zoster. Carrière, in a case of femoro-cutaneous zoster following cancer of the uterus, found parenchymatous neuritis of the nerve involved. There was no cancerous infiltration of the nerve, and Carrière attributed the neuritis to the local and direct action of cancer toxines. One of Dr. Curtin's cases was also connected with cancer of the œsophagus.

The occurrence of zoster in connection with coal-gas poisoning and as a result of the administration of arsenic presents certain problems which have not been studied with sufficient care to enable us to express any opinion. The fact that zoster or zosteriform eruptions may occur under such circumstances is established, but more cannot be said.

Wasilewsky, in his monograph on zoster as an infectious disease, cites reports of epidemics of the affection. He regards the question of immunity as settled, but with the numerous cases of recurrent zoster reported of late years, it is difficult to agree with him on this question, unless, indeed, we come to recognize the recurrent cases as zosteroid in character, rather than as true zoster.

In typical cases, prodromata, as gastric disturbance, and fever appearing several days before the eruption, with a temperature often reaching

104° F., and ceasing with the outbreak of the eruption, point, in Wasilewsky's opinion, to an infectious origin for the disease, and this view is supported by the observations of Head and Campbell, which I shall cite later.

A point in favor of the infectious character of zoster is the occurrence of enlarged lymphatic glands. Grindon and Hay have shown that true zoster is always preceded by adenopathy in the neighborhood of the eruption, or even by generalized involvement of the lymphatic glands. Hay discovered cocci in the glands.

The infectious nature of zoster having been so strongly indicated by the observations of numerous writers, it is not surprising that facts should now begin to appear in favor of its contagious character. Ferré has reported some very interesting cases in this connection. He thinks that in some cases zoster may be the consequence of a meningeal or spinal affection, and in the epidemic form may be an indication (*symptome révélateur*) of an attenuated form of cerebro-spinal meningitis. As numerous instances of the recurrence of zoster have been reported of late years, these must be taken into consideration before the infective theory is generally accepted. The view that there are several varieties of zoster, or that there is one specific zoster, an infective disease, and, therefore, not recurrent, and various zosteroid eruptions due to different causes, is one that seems to have gained considerable adherence of late years, and in the light of recent observations is certainly a plausible explanation of numerous otherwise anomalous phenomena.

The anatomy of the lesions of zoster themselves has been made the subject of investigation in the light of more recent knowledge and with the aid of modern methods. Peffer maintains that the true cause of zoster is in all cases a protozoid, which he has found in the affected skin and has described. Hartzel, who has made similar investigations, says that these protozoids are not present in ordinary inflammations of the skin, but are peculiar to zoster, variola, vaccinia, and varicella. Gilchrist, after an elaborate investigation of the subject, concludes, however, that the so-called protozoids are really the nuclei of epithelial cells.

Up to within the past year or two, Bärensprung's observations and conclusions have never been questioned, and zoster has everywhere been received as an affection closely connected with the sensory nerves, and following in its occurrence the distribution of these nerves in the skin.

It cannot have failed, however, to strike the careful observer that the eruption of zoster does not invariably follow the line of distribution of the nerves, this circumstance being particularly noticeable in thoracic zoster. Brissaud, a recent writer, goes so far as to assert that in a large number of cases the concordance of the eruption of zoster with a nerve path is a fiction.

Having made the same observation with regard to other diseases besides zoster, Brissaud sought for an explanation and found it in the theory of "metamerism."

Concluding from our knowledge of embryology that the spinal cord is composed of a series of segments superposed and relatively independent (metamers), Brissaud attempted to prove that the eruption of zoster should appear in the territory of a region innervated by a medullary metamer. This territory of innervation, however, is sometimes entirely different from that which corresponds simply to the course and distribution of the sensory nerve fibres.

Another and quite different theory of the relation of the zoster eruption to the nervous system has been proposed by Abadie. He maintains that the skin affection does not result from an alteration of the peripheral sensitive nerve fibres, nor from a medullary lesion, but from a pathological condition of the arteries and of the vasomotor nerves which regulate their dilatation in the region where the eruption is situated.

In a general way the sensory nerves accompany the arteries, at least during a portion of their course, and, therefore, the zoster eruption, which really occupies, the territory of vascular distribution, has heretofore been supposed to occupy the nerve territory. As, however, in certain localities, these two territories are neither identical nor superposable, apparent anomalies supervene, anomalies which Brissaud tries to explain by his "metameric" theory above mentioned. This hypothesis is not necessary, however, to explain the topographical anomalies of the eruption, as the cutaneous lesions occur along the bloodvessels and not along the nerve filaments.

Taking ophthalmic zoster as an example, Abadie asks how it is, if zoster is due to inflammation of the trigeminal nerve, that it only occurs (save in the very rarest cases) in the first or ophthalmic branch. As a fact, maintains Abadie, the eruption extends over the area supplied by the *supra-orbital, frontal*, and sometimes the *nasal* arteries.

The lesions of zoster, says Abadie, are due to a trophic influence proceeding from the *sympathetic nerve fibres*, which, in the case of ophthalmic zoster, follow the course of the arteries just mentioned. The pain and other nervous symptoms, which may or may not accompany the eruptions, are due to some involvement of the sensory nerves, which may be implicated in one case and may not in another.

This theory is supported by the form of the eruption in thoracic zoster. This does not occur above the line of the third intercostal space. The arteries supplying the three upper intercostal regions, instead of proceeding from the aorta, are derived from the subclavian artery, and consequently their vascular origin and that of the vasomotors which accompany them are different from the others which come directly from the aorta.

This theory of Abadie's makes clear, so he says, the apparent anomalies of the eruption which are inexplicable otherwise, but it takes away from the sensitive nerves of relation a part which does not belong to them and assigns it to the great sympathetic. It proves that the latter really commands and regulates nutrition in all the regions to which it is distributed, whether visceral or cutaneous.

We may thus understand, also, that certain forms of ophthalmic zoster may present particularly grave cerebral complications, and may be accompanied by hemiplegia, as Brissaud has shown, in some cases. The mechanism of these lesions has been difficult to explain by the nerve theory, but it is easily understood by accepting the excessive vasomotor dilatation of certain cerebral arterioles which may provoke rupture in their territories of irrigation.

Finally, Abadie says that quinine is a specific in ophthalmic zoster. Now, quinine is essentially a vasoconstrictor medicine acting on the sympathetic and producing a constriction of the arterial vessels.

These views of Abadie have not been generally accepted, although there is certainly something in them.

But, as Hallopeau says, the character of the concomitant and consecutive pains appear necessarily to imply a participation of the sensory nerves, and also the localizations can only be explained by a metameric action.

The blood examinations which have been made in zoster are worthy of mention, although their significance is not apparent. Like the microscopical examinations of the lesions, they are materials of possible future structures, but have not yet been fitted into their place.

Leredde says the white globules may fall to 3500. The polynuclears are diminished to 45 per cent. on an average; they may fall to 37 per cent. On the tenth to the twelfth day an eosinophilia of 6 to 8 per cent. has been noted.

Head and Campbell, in a recent and extremely elaborate paper, give a large number of facts regarding the origin and distribution of zoster. These investigators have been able to map out the affected areas in zoster, and have subsequently examined the spinal cord and nerves implicated. The cases in which they have been able to make post-mortem examinations number more than the sum total of those previously recorded by all other observers.

Head and Campbell find inflammatory and destructive changes in the posterior ganglia of the cord and in the Gasserian ganglion, and degeneration in the nerves leading to the skin. In mild cases the effects of these changes gradually pass away, but in severe cases the nerve fibres that have degenerated are replaced by fibrous tissue, and whole bundles of the nerve may be sclerosed.

Degeneration in the spinal cord occurs secondary to the herpetic lesion of the ganglion.

It may be noted, referring to the brain symptoms in connection with ophthalmic zoster, that the third division of the trigeminal is connected with cells in the Gasserian ganglion which send fibres centralward to lie in the so-called ascending or spinal roots.

Head and Campbell conclude that some agent, the nature of which we are ignorant, chooses the substance of the posterior root ganglion for its selected activity, producing profound inflammatory changes. These destructive changes in the ganglion give rise to irritation of its nerve elements, and to this irritation is due the eruption on the skin.

Acute inflammation of a posterior root ganglion, due to its implication in some local inflammatory process, can apparently produce an herpetic eruption indistinguishable from an eruption which arises as a manifestation of the acute specific disease (as, for instance, a case of zoster reported by Head and Campbell, where lymphosarcoma invaded the posterior root ganglion directly).

Zoster may appear in the course of gross organic disease of the spinal cord and roots. In some such cases Head thinks the original disease simply predisposes to an attack by the specific agent supposed to be the chief etiological factor in the production of the zoster.

Head has traced nerve twigs up to the portion of skin excised for examination, and found they showed marked signs of degeneration. He did not succeed in demonstrating degenerated fibres in the actual portion of skin examined.

A typical attack of zoster arises without any obvious peripheral or cerebral cause, and, as has been said, must be considered an acute specific disease of the nervous system, for it starts with a prodromal period of varying length, during which the temperature is raised. During this period the patient feels ill and has more or less pain.

If a child, he may be supposed to be sickening from one of the ordinary specific diseases. Then the rash appears, the febrile period lasting three to five days.

Head's experience with recurrent zoster is worth noting. He met with but four cases of relapse in four hundred of zoster.

In connection with the occurrence of zoster as a specific infectious disease we must consider the large number of zoster-like eruptions evidently due to various causes, as injuries, poisoning by arsenic, coal gas, etc. All these must be ruled out from the division of true zoster.

On the other hand, the occurrence of zoster as a specific fever running a regular course and characterized by a typical eruption, prepares the mind for the reception of Curtin's theory as to the involvement of various membranes and viscera.

If the cause of zoster lies in a disorganization of certain nerve cells or nerve fibres by the toxin of a specific germ, or by an unknown agent of any kind, there is some reason for admitting the possibility that the same agent may give rise to inflammatory symptoms in the pleura or in the articular cavities.

As Osler and others have described the various visceral complications of erythema multiforme, so we may regard the cases observed by Curtin as those of visceral complications of herpes zoster, and I have no doubt that when the attention of observers has been drawn to this aspect of the case we shall find numerous cases of such complications reported.

CONCLUSIONS. From what has preceded, the following conclusions may be drawn:

1. Under the designation zoster or herpes zoster is to be understood a specific infectious and possibly contagious exanthem, characterized in its invasion by lassitude, general malaise, chills, increased temperature, and more or less digestive disturbance.

Following this, in most cases, neuralgic pains develop along certain nerve-paths or metameric areas, together with the development of enlarged lymphatic glands.

After a period of several days, more or less, during which the symptoms mentioned, or some of them, have manifested themselves, the characteristic exanthem shows itself, and runs through a fixed cycle of development, acme, and decrudescence. The general symptoms, particularly the neuralgic pains, may continue during this period, or, in many cases, may diminish, usually disappearing with the eruption. In other instances, and particularly in older persons, the neuralgia may form a prolonged succedaneum to the regular course of the disease.

In a certain number of cases, probably, however, rare, various visceral complications may accompany the affection. Such are paralysis of sensory or motor nerves, inflammations of the pleura, peritoneum, articulations, or viscera.

2. The infection attacks chiefly the posterior (sensory) ganglia of the cord and the Gasserian ganglion. From thence inflammation and degeneration may extend along the nerve trunks and fibres.

No other lesions have as yet been discovered post-mortem, although it is probable that further observation will result in tracing the disease in the various membranes and viscera when its presence has been clinically noted.

The numerous examinations of the skin lesions and such blood examinations as have been made have not as yet thrown any light upon the nature of the disease.

3. Zosteroid eruptions are not infrequently observed in cases of poisoning from coal gas, after the ingestion of arsenic, following injuries of the nerves, as a result of moral shock, as grief, or in hysteria, and probably under other conditions. These, however, are to be distinguished from the true herpes zoster as defined above.

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SOME EXPERIMENTS ON THE INTERMEDIARY CIRCULATION OF THE BILE ACIDS: A CONTRIBUTION TO OUR KNOWLEDGE OF ICTERUS.

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A LARGE proportion of the bile-acid salts that are poured into the intestine from the liver are reabsorbed. This is proved by the following four series of experiments:

1. According to different authors (Bidder and Smith, and Leyden), a dog weighing 8 kg. excretes about 4 g. of bile acids in the twenty-four hours; of this amount only 0.5 to 0.7 g. will be found in the feces (Hoppe-Seyler) and unweighable traces in the urine (Naunyn, Vogel, Höne, and Dragendorff). Leyden injected 1¼ g. of one of the bile-acid salts (sodium glycocholate) into the blood of an animal and found only 0.227 g. in the twenty-four hours' urine. As the bile acids are very resistant to putrefaction in the urine and to digestive destruction in the stomach and intestine (Leyden), it cannot be assumed that they are destroyed in the bladder or the digestive tract.

2. Tappeiner placed two ligatures around a loop of intestine without disturbing its connection with its mesentery; he then placed bile-acid salts into the jejunum and the ileum at different times, and found that